

Appl. No. 09/763,616

Amendment dated: September 11, 2003

Reply to OA of: March 11, 2003

Amendments to the Specification:

On page 45, please amend the Bibliography reference 1 as follows:

*C1*

1. Howley, P.M. 1996. Papillomavirinae: The viruses and their replication. p. 2045-2076 947-978. In Field, B.N., Knipe, D.M., and P.M. Howley (eds). Field's Virology, Lippincott Raven Publ. Philadelphia.

On page 47, please amend Bibliography reference 22 as follows:

*C2*

22. Vousden, K.H., Androphy, E.J., Schiller, J.T., Lowry, D.R. Mutational analysis of bovine papillomavirus type 1 E6 protein, J. Virol. 63, 2650-2656 2340-2342(1989).

Please replace the paragraph which begins on page 4, line 3, and ends on page 4, line 8, with the following rewritten paragraph:

*C3*

Figure 1 diagrammatically depicts the E6 protein of SEQ ID NO:1 which consists of 158 amino acids, with two Cys-X2-Cys-X29-Cys-X2-Cys (SEQ ID NO:2) zinc fingers forming the most conspicuous secondary structure. Amino acid residues shown by encircled letters are conserved among HPV-6, HPV-11, HPV-16 and HPV-18. HPV-16 and HPV-18 are the most prevalent papillomaviruses in carcinomas of the cervix precursor lesions.

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Please replace the paragraph which begins on page 7, line 28, and ends on page 8, line 10, with the following rewritten paragraph:

The E6 protein of HPV-16 (Fig. 1) has a size of 158 amino acids. Its most conspicuous sequence motifs are two Cys-X2-Cys-X29-Cys-X2-Cys (SEQ ID NO:2) zinc fingers (11-13). Analysis of Swiss-Prot database indicates that this sequence motif is unique for papillomavirus E6 and E7 proteins (14), and includes numerous specific amino acids residues, highly conserved among all carcinogenic HPVs as well as many animal and human papillomavirus associated with benign lesions. The homology between all papillomavirus E6 genes permits the alignment of their nucleotide sequences, forming a useful database to establish papillomavirus taxonomy (15-17). A similar zinc finger is found in the E7 protein. The extreme conservation of E6 and E7 zinc fingers among viruses with otherwise significant sequence diversity suggests that this zinc-binding motif is required for the structure and the function of HPV E6 and E7 oncoproteins, and it has been shown that mutations affecting the HPV-16 and the bovine papillomavirus type 1 (BPV-1) E6 zinc fingers interfere with cellular transformation as well as with complex formation between E6 and E6AP and E6BP.

Please replace the paragraph which begins on page 9, line 16 and ends on page 9, line 20, with the following rewritten paragraph:

In yet a more preferred embodiment the chelated metal cation domain is a zinc domain in which the sulphhydryl groups of four cysteine residues are chelated to the zinc cation. In still yet a more preferred embodiment, the zinc domain comprises the Cys-X2-Cys-X29-Cys-X2-Cys (SEQ ID NO:2) sequence motif, wherein the zinc atom is chelated to the four Cys residues via the sulphhydryl groups (see Figure 1).

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Please find attached at the end of this Amendment a paper copy of a Sequence Listing as required by the Examiner in the Official Action. Please insert the paper copy of the Sequence Listing immediately after the drawings.